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voltages comprises means for applying voltages to accelerate ions from outside said ion guide into said ion guide.

Remarks

Receipt is acknowledged of the Office Action of November 16, 1998. Reconsideration of the application and a three month extension of the time provided for response to the final Office Action are respectfully requested. The Commissioner is hereby authorized to debit our deposit account, Account No. 02-2105, for the extension fees, the fee for the new claims, the fee for the Information Disclosure Statement (IDS), the terminal disclaimer fee, and any other amounts that may be required.

Counsel would like to thank the Examiner for the courtesy he showed to counsel and to Applicant Craig Whitehouse in the interview of February 9, 1999. Further thereto, Applicant has amended the claims as set forth above to clarify and more distinctly claim the non-obviousness of the inventions over the cited references. It is believed that all of the claims are in patentable form.

In the interview, the Franzen reference (U.S. Patent No. 5,763,878) and the Douglas reference (EP 529,885) were discussed with the Examiner. In the November 16th Office Action, the Examiner had suggested that if collisional gas is used in multipole ion guide 12 of the Franzen reference, as taught by the secondary Douglas reference, then one may achieve fragmentation of ions located in that multipole ion guide. As discussed in the interview, however, Applicant respectfully points out that Frantzen distinctly teaches away from adding collision gas to multipole ion guide 12. For example, in Frantzen's description of his device

71

he expressly indicates that cooling within the multipole ion guide arrangement (12) by using a collisional gas therein is considered by him to to be very disadvantageous. See, Column 3, lines 43-60. Frantzen explains that adding collision gas to the multipole ion guide 12 would be incompatible with the low vacuum pressure requirements of the TOF flight tube. Thus, in the section where he describes the disadvantages of prior techniques he indicates that the presence of collision gas in a three dimensional quadrupole ion trap will reduce the repetition rate of the procedure to about 20 to 100 spectra per second – a very significant loss of sensitivity since a repetition rate of 10,000 spectra per second is desirable. See, Column 2, lines 6-19. Likewise, in his detailed description, Frantzen explains that MS/MS analyses become possible if the time-of-flight spectrometer is provided with a corresponding collision chamber for fragmentation, thereby further implying that he does not contemplate fragmentation within the multipole ion guide 12. See, Column 7, lines 1-8.

Similarly, it should be noted that the diaphragms in Frantzen cited by the Examiner surround the multipole ion guide 12, which is in the pulsing region. However, since Frantzen teaches away from placing pressure in that multipole ion guide 12 (as discussed in the previous paragraph), the reference provides neither a teaching or a suggestion of conducting fragmentation in that ion guide.

Accordingly, it is clear that Frantzen does not teach or suggest using the multipole ion guide for fragmentation, as is Applicant's invention in apparatus Claims 33, 90, and the dependents thereon. Thus, it is believed that the inventions of apparatus Claims 33 and 90 (relating to fragmentation) are not obvious over the cited references, as those references neither teach nor suggest the subject matter of the claimed inventions. The Examiner did not

indicate that any of the references show mass selection within a TOF multipole ion guide, and thus, Claims 62 and 90 are also believed to be non-obvious over the cited art.

Amendments to the Claims

To clarify the scope of the inventions of the present application, the claims have been amended as set forth above. As recited in the amended claims, new apparatus and methods are provided for fragmentation and/or mass selection of ions within the multipole ion guide of a Time-Of-Flight mass spectrometer.

By way of background, means have long been provided for applying voltages to a multipole ion guide. Such means for providing voltages, i.e. a power supply and electronics for controlling the power supply, are well known in the art. Previous to the present inventions, however, Time-Of-Flight mass spectrometers with a multipole ion guide therein have only been provided with means for applying voltages to the guide so as to direct ions through the guide or trap ions within the guide. These embodiments, for example, are recited in the patents and parent applications recited above, including U.S. Patent No. 5,652,427 and U.S. Patent No. 5,689,111.

In the present application, an improved Time-Of-Flight (TOF) mass spectrometer is provided which has features not taught or suggested in the cited references. This TOF mass spectrometer has further means for applying voltages provided therein, in addition to the means for providing the primary voltage which is used to direct ions through the guide or to trap ions in the guide. These further means are used to add additional voltages to the multipole ion guide so as to fragment ions within the guide (as recited in Claims 33 and 90)

and/or to mass select ions located within the guide (as recited in Claims 62 and 90). Accordingly, the present inventions result in an improved apparatus with additional functions not available with the devices of the prior art. The claimed devices allow a range of useful experimental techniques, as described in the specification, which greatly enhance the analytical capabilities of a Time-Of-Flight mass spectrometer.

These embodiments of the inventions are recited in the amended apparatus claims above. As recited therein, the claimed apparatus includes a means for providing a primary RF voltage or a means for providing a voltage which is used to direct the ions through a desired trajectory within the guide (i.e. a trajectory which either passes the ions through the guide or traps them within the guide). In addition, the apparatus also includes further, additional, means for providing voltages which will cause fragmentation and/or mass selection of the ions within the multipole ion guide.

None of the references cited in the prior Office Actions teach or suggest a Time-Of-Flight mass spectrometer with a multipole ion guide located therein, which has both a means for application of a primary voltage (to direct ions through the guide or trap ions in the guide), and also has additional means for applying additional voltages to fragment ions while they are within the guide (as in Claims 33 and 90) and/or to mass select ions while they are within the guide (as in Claims 62 and 90). Accordingly, it is believed that the inventions of the amended apparatus claims and all of the dependents thereon are fully patentable.

Similarly, the method claims set forth in the prior Amendment are all believed to be patentable over the cited references. This is due to the fact that none of the references teach or

suggest any methods which include the steps of conducting fragmentation and/or mass selection of ions within a multipole ion guide of a Time-Of-Flight mass spectrometer. Accordingly, as none of the references teach or suggest these methods, the method claims are all believed to be patentable.

In addition to the above, it is to be noted that the several minor amendments to the method claims have been made merely to improve their clarity, and not to recite any distinctions over the references of record. Also, with respect to all of the claims, it should be noted that, although the claims often refer to elements in the singular, the use of the transition "comprising" in the claims is meant to indicate that the claims are open claims. Thus, the claims are also intended to include embodiments in which a plurality of any particular claimed element is present. For example, where the claims refer to "a" multipole ion guide, it is to be understood that the intention herein is to include apparatus with multiple multipole ion guides, as well. The use of the occasional plural (e.g. "at least one vacuum pumping stage") in the claims is intended to provide antecedent basis for dependent claims which explicitly refer to a plurality of that particular element (e.g. "a subsequent one of said vacuum pumping stages") and to expressly include the embodiment wherein the multipole ion guide is located within one or more vacuum pumping stages.

Information Disclosure Statement

An Information Disclosure Statement (IDS) is enclosed with various references cited therein, including a patent which was recently issued by the Patent Office, U.S. Patent No.

5,847,386, issued on December 8, 1998 to Thomson and Jolliffe ("the '386 patent"). As discussed in the IDS, and as evidenced by the documentation from the file wrapper of the '386 patent (attached hereto), the priority date of the present application predates that of the '386 reference. On its face, the patent appears to indicate that it has an earlier filing date than the present application. However, the file wrapper shows that an error was made by the PTO on the front page and first page of the specification of the '386 patent, listing the wrong priority application filing date. Accordingly, the reference is not believed to be available for citation against the subject matter of the present application.

Double Patenting Rejection

A terminal disclaimer is enclosed with respect to the Whitehouse patent (U.S. Patent No. 5,652,427) and the Dresch patent (U.S. Patent No.5,689,111), both of which are assigned to Analytica of Branford, Inc., the assignee of the present application. The terminal disclaimer overcomes the double patenting rejection raised by the Examiner in the Office Action.

Amendment to Add Priority Claims

The present application has been amended to claim the priority of the Whitehouse patent and the Dresch patent, and the applications associated with those patents, including their parent and continuation applications. Those patents and applications disclose analytical instruments in the form of Time-Of-Flight mass spectrometers with multipole ion guides therein. The present application, which provides the improvements of devices and methods for fragmentation and/or mass selection of ions within the multipole ion guide, should be

regarded as a continuation-in-part of those patents and applications. The present application complies with the formal requirements of 35 U.S.C. §120 to be considered a continuation-in-part application in that: (a) the prior applications and the present application have at least one common inventor; (b) the present application was filed before the patenting or abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application; and (c) the present application contains or is amended to contain a specific reference to the earlier filed application. As a result, it is requested that these additional claims of priority be entered into the file wrapper.

Amendment to the Specification and Drawings

Further to the Examiner's request in the Office Action, the lengthy specification has been amended to correct several minor errors therein, such as typographical and grammatical matters. In addition, the drawings have been corrected to add a missing reference numeral referring to the quadrupole 108. No new matter has been added.

Accordingly, in view of the above, it is submitted that the present application is in a condition suitable for allowance. A favorable Office Action allowing all of the claims is respectfully requested.

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Respectfully submitted,

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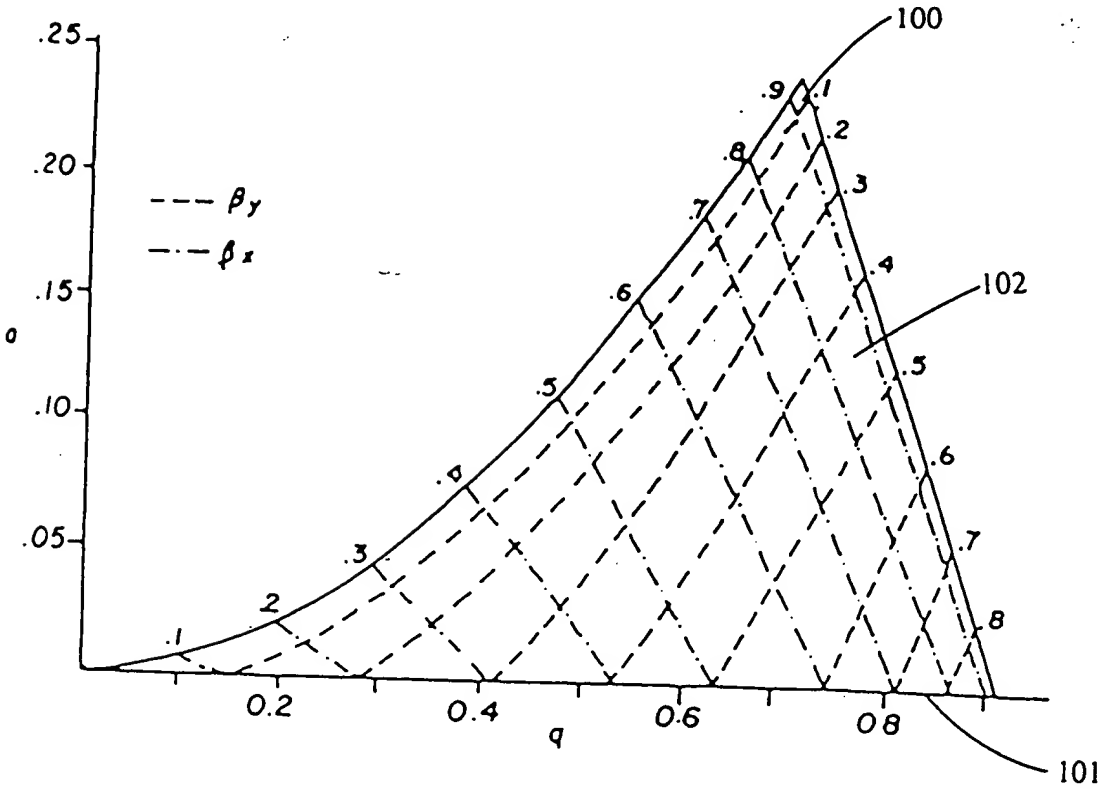

Figure 9

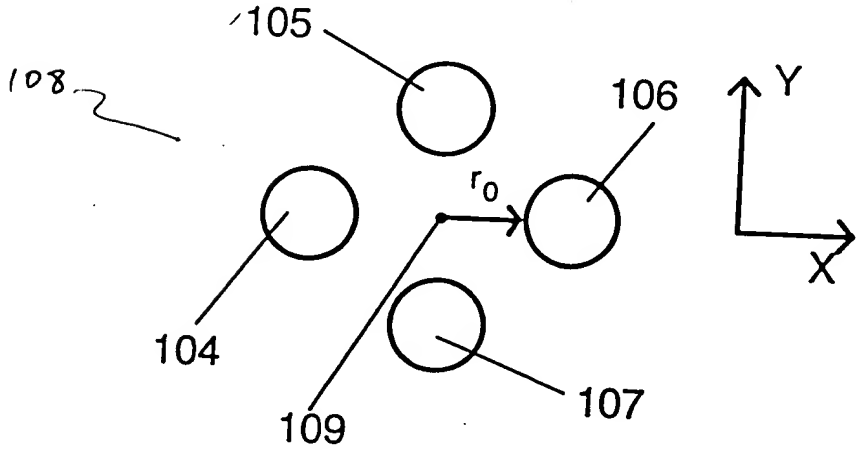

Figure 10